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| 10/686,713      | 10/17/2003  | Michelle M. Hanna    | 2072.0010006        | 9587             |

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| EXAMINER |
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KIM, YOUNG J

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| ART UNIT | PAPER NUMBER |
|----------|--------------|

1637

DATE MAILED: 06/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/686,713

**Applicant(s)**

HANNA, MICHELLE M.

**Examiner**

Young J. Kim

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 136-147 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 136-147 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 October 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>3/7/05</u> . | 6) <input type="checkbox"/> Other: ____.  |

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## **DETAILED ACTION**

### ***Preliminary Remark***

The Preliminary Amendment received on October 17, 2003, canceling claims 1-135 and adding claims 136-147 is acknowledged.

### ***Information Disclosure Statement***

The IDS received on March 7, 2005 is acknowledged.

A signed copy of its PTO-1449 is enclosed herewith.

### ***Drawings***

The drawings received on October 17, 2003 are acceptable.

### ***Sequence Compliance***

The application contains several Figures which recite nucleotide sequences which must comply with rules set forth in 37 CFR 1.821 through 1.825. For example, Figure 30 discloses a nucleotide sequence having a sequence of more than 10 contiguous nucleotides without a proper SEQ ID identifier.

A fully responsive amendment must contain response to all objections/rejections made herein, a CRF (computer readable medium), a paper copy of the sequence listing, a statement under 37 CFR 1.821(f).

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 136, 137, 145, and 146 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 136 is indefinite for reciting the phrase, “abortive reiterative synthesis,” because the specification does not explicitly define what constitutes an abortive reiterative synthesis, so as to properly determine the metes and bounds embraced by this limitation.

Claims 137, 145, and 146 are indefinite by way of their dependency on claim 136.<sup>1</sup>

Claim 146 is indefinite because the method is for detecting the presence of a target molecule, wherein the detection is achieved by detecting multiple copies of detectable oligonucleotides (i.e. nucleic acid), but claim 146 recites that the target molecule being detected is a protein.

No assumption could be made for this claim for the purpose of further prosecution on its merits.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 136-138, 140, and 145-147 are rejected under 35 U.S.C. 102(b) as being anticipated by Sasaki et al. (PNAS USA, March 1998, vol. 95, pages 3455-3460).

Sasaki et al. disclose a transcriptional sequencing method, said method comprising the steps:

a) synthesizing multiple copies of detectable oligonucleotides through abortive reiterative synthesis on a nucleic acid template (accomplished by a nucleic acid template comprising a T7 promoter sequence T3 promoter sequence and RNA polymerase; see Figure 4 on page 3457, wherein the abortive reaction is achieved by incorporation of four kinds of dye-3' dNTPs);

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b) detecting said oligonucleotide, thereby determining the sequence (or presence) of said target molecule (page 3457, 2<sup>nd</sup> column, Figure 4 description), thereby clearly anticipating claim 136.

With regard to claim 137, the artisans employ RNA transcription on a DNA template comprising promoter sequences (page 3455, 2<sup>nd</sup> column, bottom paragraph; page 3456, 1<sup>st</sup> column bottom paragraph through 2<sup>nd</sup> column, 1<sup>st</sup> paragraph).

With regard to claim 138, the method involves the incubation of DNA template with an initiator (primers comprising T7 promoter sequence and T3 promoter sequence), followed by the incubation with RNA polymerase (see Figure 4), followed by the detection of the synthesized multiple reiterative oligonucleotide transcripts (by sequencing).

With regard to claim 140, the transcript termination is achieved through incorporation of a nucleotide analog, dye-3' dNTPs (fluorescent dye terminators; *see* page 3457, 1<sup>st</sup> column, bottom paragraph).

With regard to claim 145, the target molecule is a nucleic acid (page 3456, 2<sup>nd</sup> column, 1<sup>st</sup> paragraph).

With regard to claim 147, the nucleic acid template comprises a structure which allows the abortive reiterative synthesis to occur. Since the specification does not have a specific definition of what is considered to be an "abortive promoter cassette," and since the claims do not recite a structure of such cassette, based on a reasonable broadest interpretation of the claim, any structure which comprises promoter sequence that is capable of effecting abortive reiterative synthesis, is deemed to meet this limitation.

Therefore, Sasaki et al. clearly anticipate the invention as claimed.

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<sup>1</sup> Claim 138, while dependent on claim 136, further defines what steps are to be conducted in an abortive RNA

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Claims 136-139, 141-145, and 147 are rejected under 35 U.S.C. 102(b) as being anticipated by Daube et al. (Science, November 1992, vol. 258, pages 1320-1324).

Daube et al. disclose a method of detecting the presence of a target molecule, said method comprising the steps:

a) synthesizing multiple copies of detectable oligonucleotides through abortive reiterative synthesis on a nucleic acid template (page 1321, 1<sup>st</sup> column, bottom paragraph; 2<sup>nd</sup> column, and 3<sup>rd</sup> column); and

b) detecting said oligonucleotides (page 1322, Figures 3 and 4), thereby clearly anticipating claim 136.

With regard to claims 137-139, the reiterative synthesis is abortive RNA transcription on a DNA template (page 1320, 3<sup>rd</sup> column, 2<sup>nd</sup> paragraph and Figure 1 on page 1321), wherein the termination is terminated by nucleotide deprivation (page 1322, 1<sup>st</sup> column, wherein the synthesis is halted by use of only three of the four nucleotides).

With regard to claim 141, the artisans disclose that the read-through does occur, which the synthesis is halted by encountering a termination sequence (page 1322, 2<sup>nd</sup> column, 2<sup>nd</sup> paragraph and page 1321, 3<sup>rd</sup> paragraph, in the phrase, "most of the initiating polymerases do indeed synthesize processively to the end of the template strand...[t]his was demonstrated by the accumulation of RNA products that were 68 to 72 nt in length, with 72 nt corresponding to the expected full-length product.").

With regard to claims 142-144, the bubble complex formed by the artisans require a non-template strand of hybridized to the template DNA strand, at a specific region on the DNA template so as to start the transcription reaction (see Figure 1), wherein the bubble complex is

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transcription, and thus is held definite.

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formed by the first double-stranded region, a second region of two unpaired strands, and a third region which is a double-stranded (upstream duplex; bubble; and downstream duplex, Figure 1).

With regard to claim 145, the target molecule is a nucleic acid (i.e., DNA).

With regard to claim 147, the nucleic acid template comprises a structure which allows the abortive reiterative synthesis to occur. Since the specification does not have a specific definition of what is considered to be an "abortive promoter cassette," and since the claims do not recite a structure of such cassette, based on a reasonable broadest interpretation of the claim, any structure which comprises promoter sequence that is capable of effecting abortive reiterative synthesis, is deemed to meet this limitation.

Therefore, the invention as claimed is clearly anticipated by Daube et al.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 140 is rejected under 35 U.S.C. 103(a) as being unpatentable over Daube et al.

(Science, November 1992, vol. 258, pages 1320-1324) in view of Sasaki et al. (PNAS USA, March 1998, vol. 95, pages 3455-3460).

The teachings of Daube et al. have already been discussed above.

Daube et al., in achieving termination of transcription, does not explicitly disclose the use of a nucleotide analog for termination.

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Sasaki et al. disclose a well known method of employing chain terminating nucleotides (page 3457, 1<sup>st</sup> column, bottom paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Daube et al. with the teachings of Sasaki et al., thereby arriving at the claimed invention for the following reasons.

Daube et al., in analyzing the terminated transcripts, involve radioactive labeling of the transcripts, wherein the transcripts are analyzed by electrophoresis.

Thus, one of ordinary skill in the art would have been reasonably motivated to employ a more environmentally safer alternatives, such as fluorescently labeled nucleotide chain terminators, so as to aid in the detection of the terminated transcripts, for the well known and established benefits of using fluorescently labeled nucleotide chain terminators, such as higher sensitivity, and environmentally safer products. One of ordinary skill in the art would have had a clear expectation of success at the combination since the use of chain terminating, fluorescently labeled nucleotides are commonly employed in nucleic acid sequencing reactions which require the transcription to be terminated at the site of its incorporation.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686



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F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 136-147 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-34 of U.S. Patent No. 7,045,319. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the issued patents are narrower species of method which renders the broader claims of the instant application in a genus-species anticipatory way.

Claims 136-147 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 26, 27, 103, 112, and 136-139 of copending Application No. 10/488,971 (herein, the '971 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims of the '971 application are narrower species of method which renders the broader claims of the instant application in a genus-species anticipatory way.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 136-147 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-22, 32-34, and 44 of copending Application No. 10/976,240 (herein, the '240 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application and the

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claims of the '240 application require the same method of reiteratively synthesizing oligonucleotide transcripts which are terminated, as well as employing an abortive promoter cassettes.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 136-147 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-27 of copending Application No. 10/425,037. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims of the instant application and the claims of the '240 application require the same method of reiteratively synthesizing oligonucleotide transcripts which are terminated, as well as employing an abortive promoter cassettes.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 136-147 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over pending (and/or elected) claims of copending Application No. 10/600,045; 10/602,045; and 10/607,136. Although the conflicting claims are not identical, they are not patentably distinct from each other because as reasons already set forth above.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Conclusion***

No claims are allowed.

### ***Inquiries***

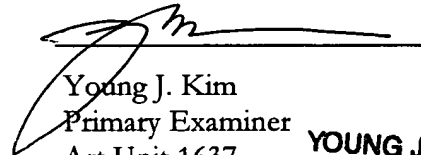
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is

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on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m. The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

  
Young J. Kim  
Primary Examiner  
Art Unit 1637  
6/9/2006  
**YOUNG J. KIM**  
**PATENT EXAMINER**

yjk